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14. ABSTRACT Chlorosulfonyl isocyanate (CSI) is known to react with hydrocarbon alkenes by a stepwise pathway. Kinetic studies and quantum chemical calculations show that (CSI) reacts by a concerted process with monofluoroalkenes that have a calculated vertical ionization potential (IP) value > 8.9 eV. Monofluoroalkenes however, with IP values < 8.5 eV react with CSI by a stepwise process similar to hydrocarbon alkenes. Kinetic data and quantum chemical calculations also support a pre-equilibrium complex on the reaction pathway just before the stepwise or concerted kinetic transition states. The synthetic utility of CSI reactions with unreactive hydrocarbon and monofluoroalkenes is enhanced by running the reactions at a lower temperature where the pre-equilibrium is shifted toward the complex.					
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Kinetic data and quantum chemical calculation studies on the stepwise vs. concerted pathways for reaction of chlorosulfonyl isocyanate reactions with monofluoroalkenes

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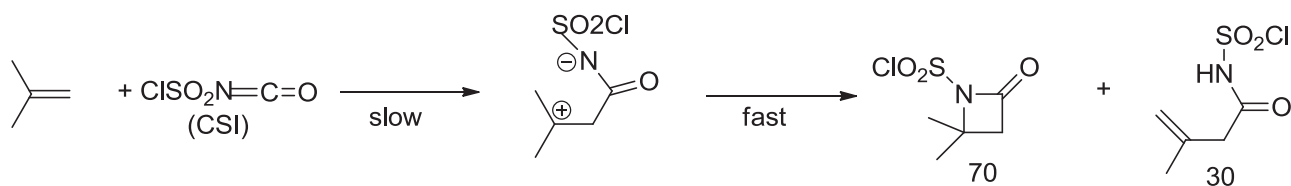
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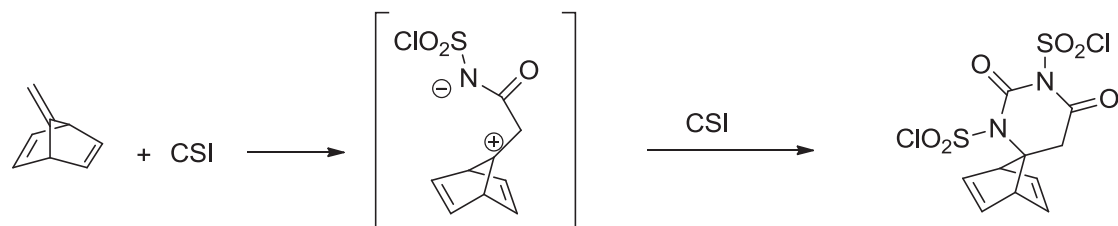
21st Winter Fluorine Conference, January 17, 2013

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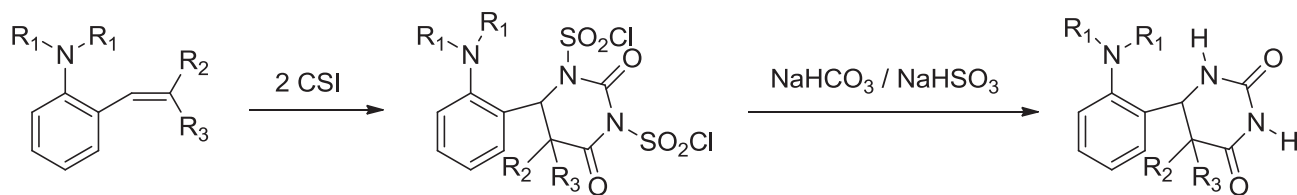
Stepwise Reactions of Chlorosulfonyl Isocyanate (CSI) with Hydrocarbon Alkenes



R. Graf, *Justus Liebigs Annalen der Chemie*, **1963**, 661, 111-157.



Paquette, L. A. and Broadhurst, M. J., *J. Org. Chem.*, **1973**, 38, 1893-1902.



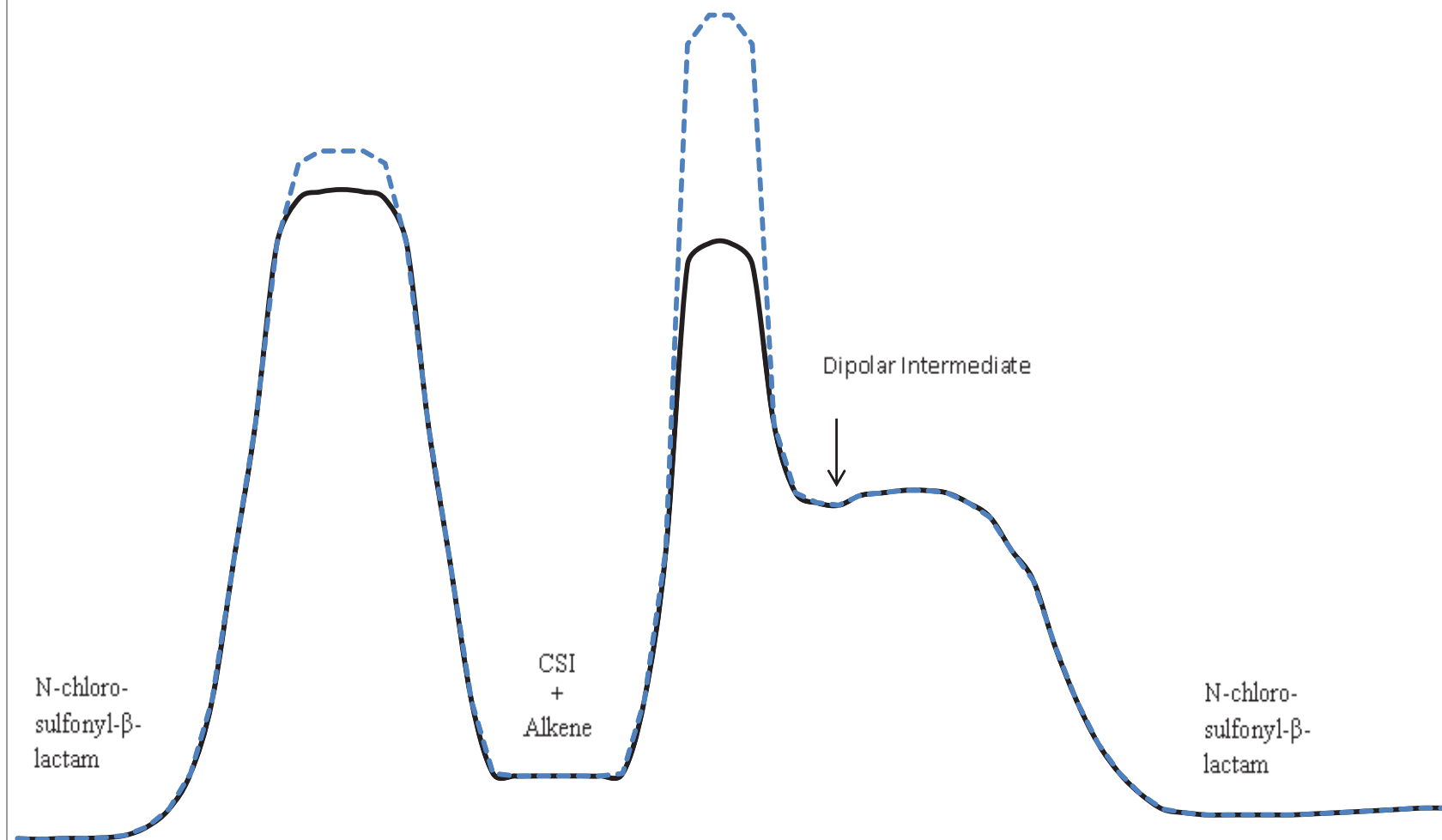
Hollywood, F. and Suschitzky, H., *Synthesis*, **1982**, 662-665.

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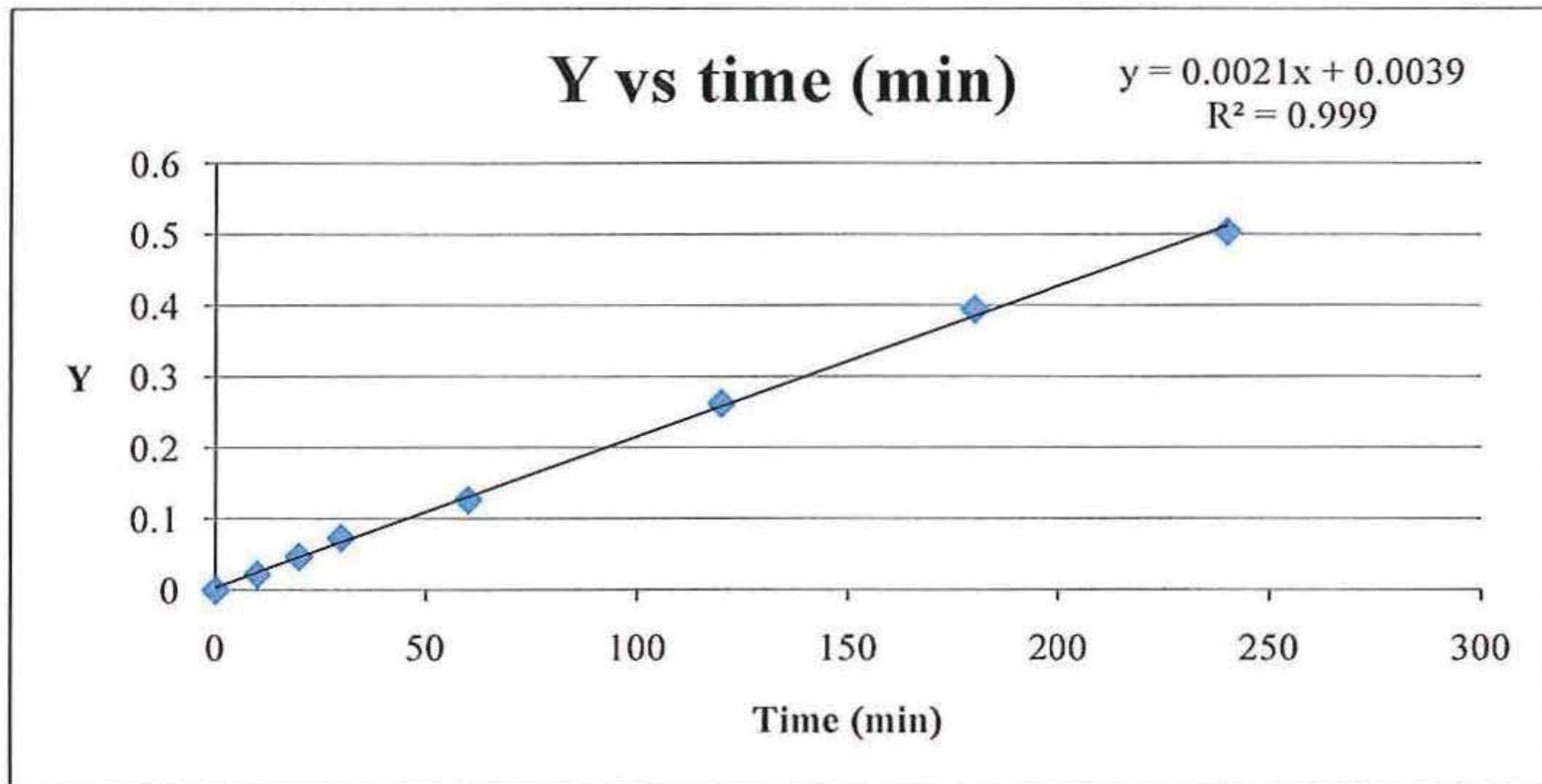
Free Energy vs. Reaction Coordinate Diagram

Solid line: Pathways available to hydrocarbon alkenes with CSI

Dashed line: Pathways available to monofluoroalkenes with CSI



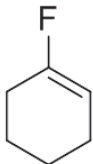
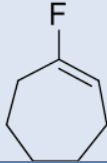
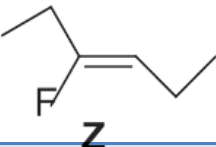
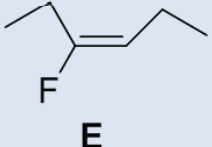
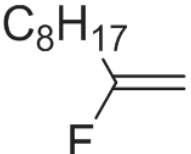
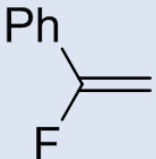
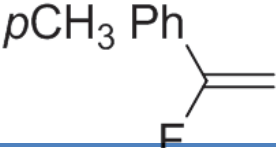
Reaction of 1-fluorocyclohexene with CSI at 28.6 °C in CH₂Cl₂



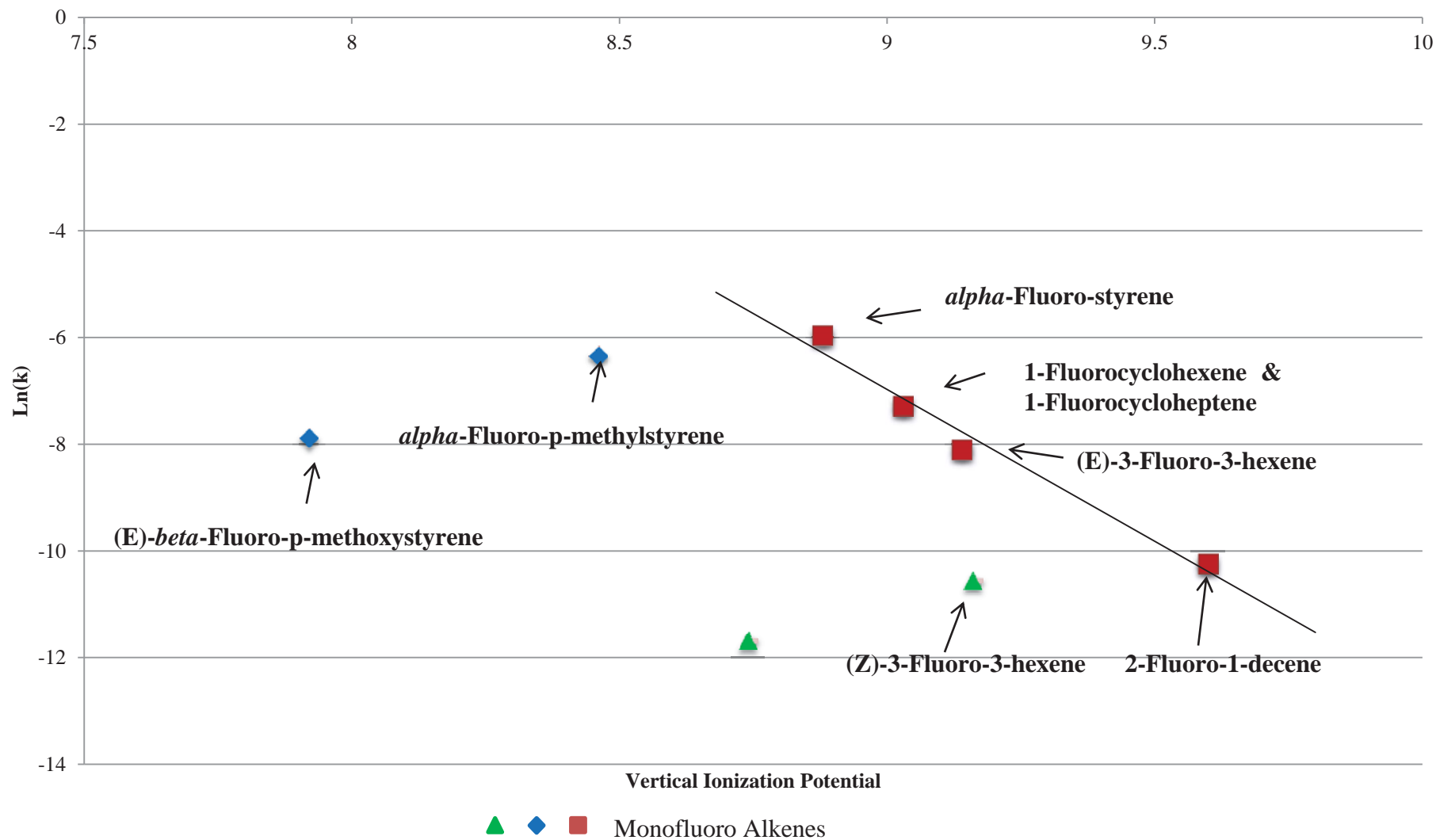
$$Y = (1/b_o - a_o) \ln a_o(b_o - x)/b_o(a_o - x)$$

$$k = 3.5 \pm 0.1 \times 10^{-5} \text{ l/mol s}$$

Fluoroalkene**Rate Constants (l/ mol s) @ 28.6° C**

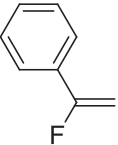
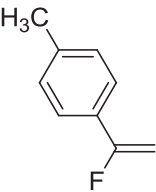
	$3.5 \pm 0.1 \times 10^{-5}$
	$5.0 \pm 0.4 \times 10^{-4}$
 Z	$2.6 \pm 0.4 \times 10^{-5}$
 E	$2.9 \pm 0.1 \times 10^{-4}$
 C_8H_{17}	$3.6 \pm 0.3 \times 10^{-5}$
 Ph	$3.7 \pm 0.4 \times 10^{-3}$
 pCH_3 Ph	$1.8 \pm 0.08 \times 10^{-3}$

Natural Log of Rate Constants vs. Ionization Potential ^a

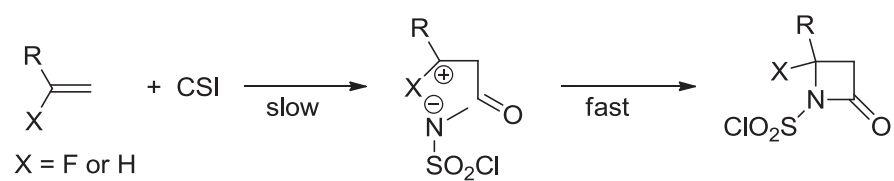


^aIonization Potentials calculated at the MP2/ 6-311G (d,p) level.

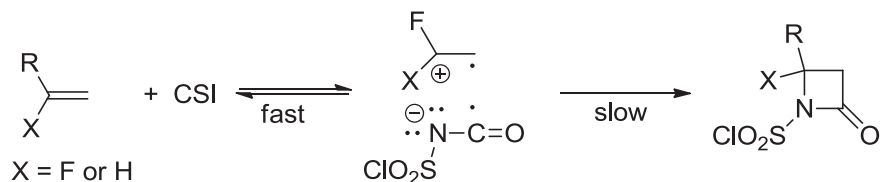
Reaction Progress of Chlorosulfonyl Isocyanate (CSI) with Alkenes

<u>Alkene</u>	<u>Time for Completion at Room Temperature</u>	
	<u>With TEMPO</u>	<u>Without TEMPO</u>
	No Effect	No Effect
	60 % Reacted in 20 hrs.	Complete in 5 min.

Previously Accepted Stepwise Dipolar Pathway



Formation of a Pre-Equilibrium SET Intermediate for the Stepwise pathway of CSI with Hydrocarbon Alkenes and Monofluoroalkenes with IP < 8.5 eV



Monofluoroalkene

(1) *alpha*-Fluorostyrene and *beta*-fluoro-*p*-methoxystyrene show intense color on mixing with CSI with absorbances at 642 and 505 nm, respectively. Their absorbance increases as the temperature is decreased to 0 °C.

(2) Rate constants for *alpha*-fluoro-*p*-methylstyrene (stepwise).

$$k = 1.8 \times 10^{-3} \quad @ \ 28.6 \text{ } ^\circ\text{C}$$

$$k = 2.3 \times 10^{-3} \quad @ \ 14.9 \text{ } ^\circ\text{C}$$

Hydrocarbon Alkene

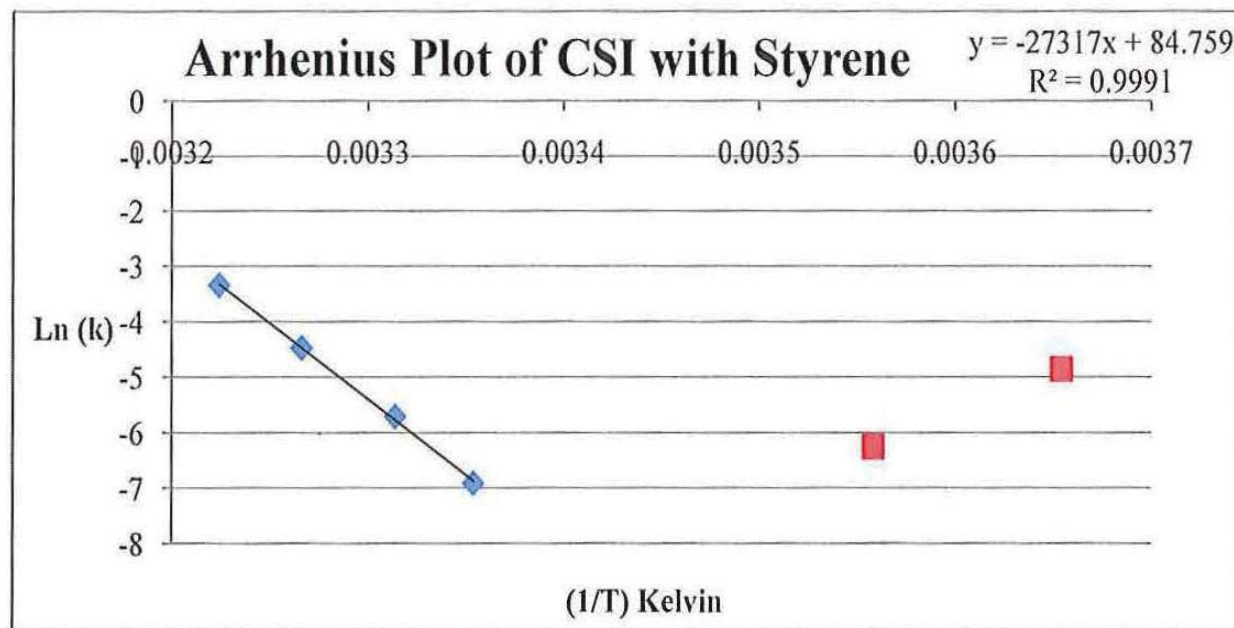
(1) Rate constants for styrene.

$$k = 1.0 \times 10^{-3} \quad @ \ 25 \text{ } ^\circ\text{C}$$

$$k = 7.8 \times 10^{-3} \quad @ \ 0.5 \text{ } ^\circ\text{C}$$

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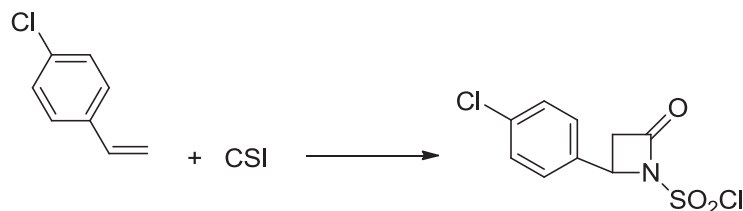
T (°C)	T (Kelvin)	1/T	k (L/(Mol*min))
0.5	273.65	0.0037	0.408137143 0.515116755 0.486444945
7.9	281.05	0.0036	0.113142697 0.097397185 0.135863429
25	298.15	0.0034	0.06
28.6	301.75	0.0033	0.198686645 0.200637868 0.199203428
33	306.15	0.0033	0.620570278 0.706671287 0.740754416
37	310.15	0.0032	2.095476629 2.159157419 2.128805932



slope	-27317			
Ea	54279 cal/mol	cal/mol	h	6.62607E-34
ΔH	53673 cal/Mol	cal/mol	K	1.38066E-23
			R	1.987

^a Data from Clauss, K. *Liebigs Ann. Chem.* 1969, 722, 110.

CSI Reaction with *p*-Chlorostyrene



<u>Solvent</u>	<u>T (°C)</u>	<u>Reaction time</u>	<u>% Yield</u>
CH ₂ Cl ₂	55°	18 hrs	40 ^a
CH ₃ NO ₂	25°	16 hrs	25 ^b
CH ₃ NO ₂	0°	5 min	80 ^b

^a Isolated yield.

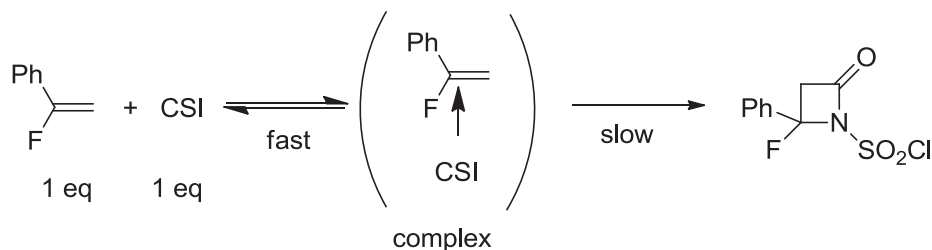
^b Percent yield by ¹⁹F NMR with 4-fluoroanisole as standard.

Yield at room temperature in nitromethane is poor because N-chlorosulfonyl-β-lactam rearranges.

Formation of a Pre-Equilibrium Complex for Concerted Reactions of Monofluoroalkenes with IP values > 8.9 eV

1. A complex rather than an SET intermediate is proposed for the concerted reaction because:
 - (a) TEMPO has no effect on the concerted reaction of CSI with *alpha*-fluorostyrene.
 - (b) The intense color on mixing CSI with *alpha*-fluorostyrene is not observed.
2. The rate increases at lower temperature for the concerted reaction of CSI with *alpha*-fluorostyrene because the equilibrium shifts toward the complex.
3. The synthetic utility for the concerted reaction of CSI with *alpha*-fluorostyrene is also improved as the equilibrium shifts toward the complex at lower temperatures.
4. Quantum Chemical Calculations show complexes of CSI with 2-fluoro-1-decene and *alpha*-fluorostyrene that are -6.0 and -6.7 kcal/mole more thermodynamically stable than their dissociated free reagents.

α -Fluorostyrene Concerted

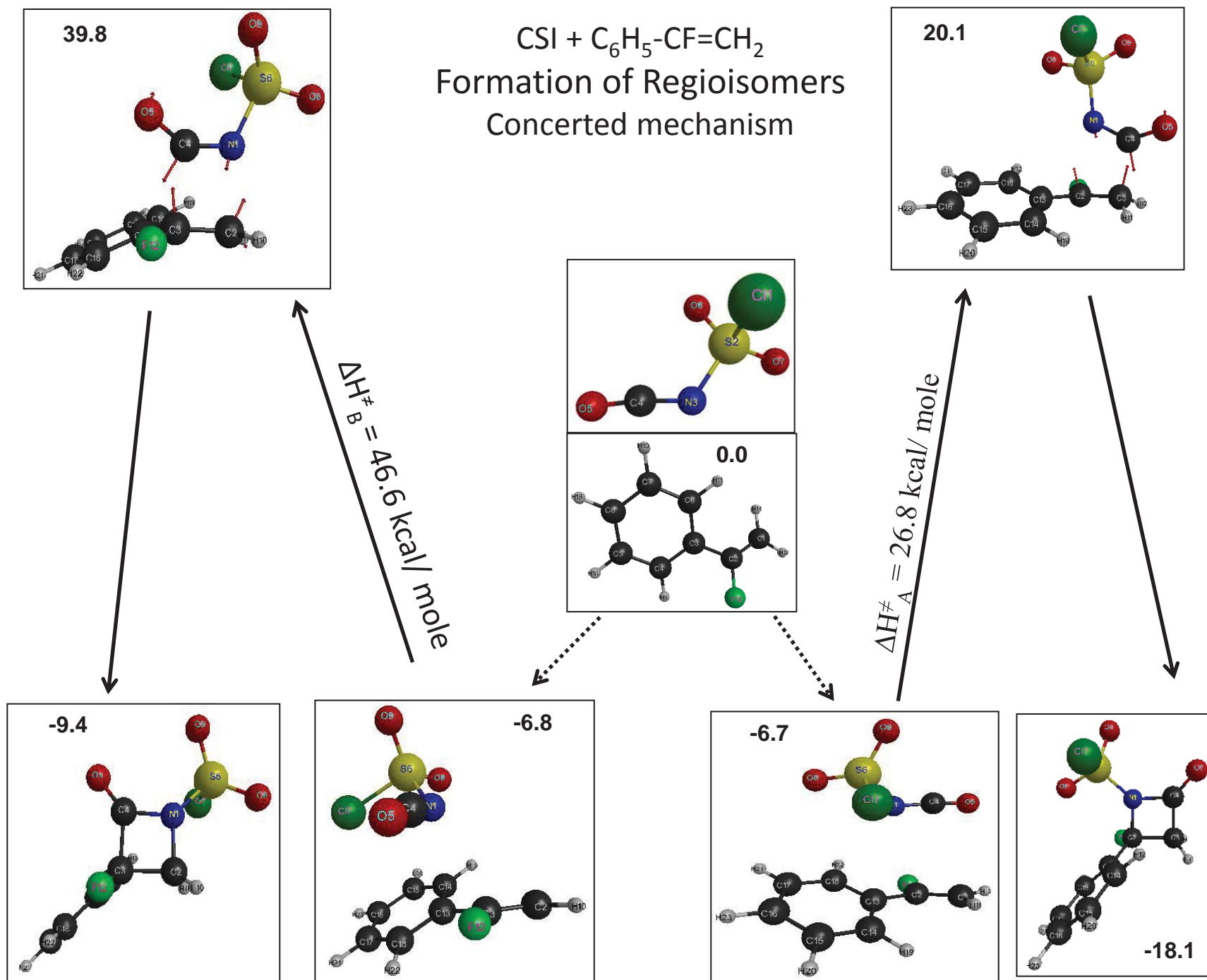


<u>Solvent</u>	<u>T (°C)</u>	<u>Reaction Time</u>	<u>Percent Yield^a</u>
CH ₂ Cl ₂	25°	4 hrs	45 ^b
CH ₂ Cl ₂	0°	4 hr	25
CH ₂ Cl ₂	- 10°	0.75 hr	35
CH ₂ Cl ₂	- 15°	0.5 hr	60
CH ₂ Cl ₂	-20°	0.75 hr	50

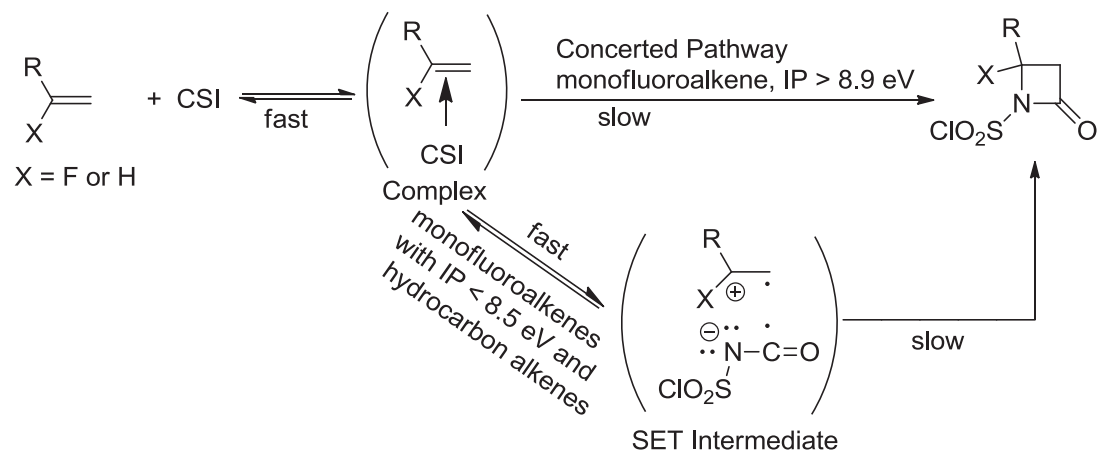
^a Percent yield by ¹⁹F NMR with 4-fluoroanisole as standard.

^b Shellhamer, *et. al.* *J. Org. Chem.*, **2010**, 75, 7913.

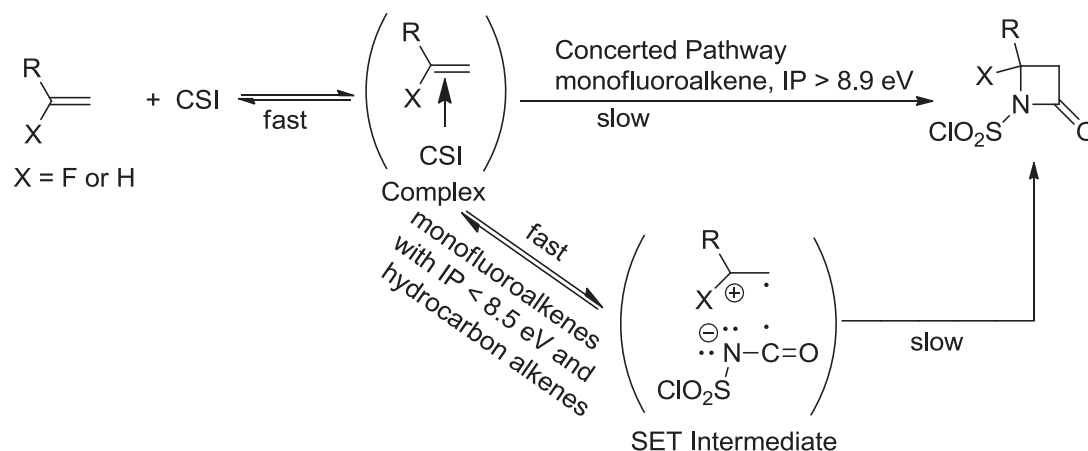
CSI + C₆H₅-CF=CH₂
Formation of Regioisomers
Concerted mechanism



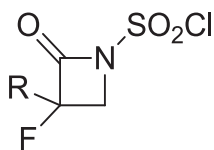
Postulated Concerted and Stepwise Dipolar Single Electron Transfer (SET) Pathways



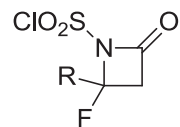
Postulated Concerted and Stepwise Dipolar Single Electron Transfer (SET) Pathways

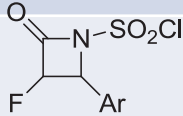
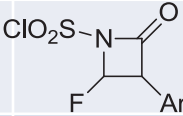


The SET pathway may be the norm. Perhaps the concerted pathway can only occur when the oxidation potential of the electron-deficient monofluoroalkenes ($\text{IP} > 8.9 \text{ eV}$) is too high and it does not allow for the Single Electron Transfer process from the monofluoroalkene.



Enthalpies of Activation (concerted rxns)



ΔH_B (kcal/mol)	$RCF=CH_2$	kcal/mole	
		ΔH^\ddagger_A	$\Delta\Delta^\ddagger_{B-A}$
46.6	$C_6H_5-CF=CH_2$	26.8	19.8
46.4	<i>para</i> $CH_3-C_6H_4-CF=CH_2$	24.3	22.1
47.2	<i>para</i> $CH_3O-C_6H_4-CF=CH_2$	23.9	23.3
47.4	$C_8H_{17}-CF=CH_2$	26.1	21.3
34.8	<i>Z</i> $C_2H_5-CF=CH-C_2H_5$	24.3	10.5
37.1	<i>E</i> $C_2H_5-CF=CH-C_2H_5$	25.3	11.8
	$CHF=CHAr$		
36.8	<i>E</i> $C_6H_5-CH=CHF$	33.3	3.5
35.3	<i>E para</i> $CH_3-C_6H_4-CH=CHF$	34.0	1.3
34.9	<i>E para</i> $CH_3O-C_6H_5-CH=CHF$	35.1	- 0.2
40.2	<i>E para</i> $Cl-C_6H_4-CH=CHF$	35.7	4.5
42.3	<i>E para</i> $CF_3-C_6H_4-CH=CHF$	37.0	5.3

CONCLUSION

1. Monofluoroalkenes react with CSI by either a concerted ($IP > 8.9$ eV) or by a dipolar stepwise SET ($IP < 8.5$ eV) pathway.
2. Hydrocarbon alkenes react with CSI by the SET dipolar pathway rather than the previously accepted dipolar pathway.
3. Concerted reaction of CSI with monofluoroalkenes that have IP values > 8.9 eV form a complex just before the rate determining step as indicated by:
 - (a) an increase in their rate constants at lower temperature as the equilibrium shifts toward the complex.
 - (b) the improved synthetic utility at lower temperature because the equilibrium shifts toward the complex.
 - (c) quantum chemical calculations show the formation of complexes.

Conclusions continued

4. Electron-rich monofluoroalkenes ($IP < 8.5 \text{ eV}$) and hydrocarbon alkenes react by a stepwise pathway through an SET intermediate as indicated by:
 - (a) The effect of TEMPO to significantly interrupt the reaction progress.
 - (b) The intense color of the SET intermediate from electron-rich monofluoroalkenes that increases in absorbance as the temperature is decreased.
 - (c) The SET intermediate must also be on the reaction pathway before the slow step as indicated by:
 - i) an increase in the reaction rate constants at lower temperatures as the equilibrium shifts toward the complex.
 - ii) the improved synthetic utility of the reactions at lower temperature because the equilibrium shifts toward the complex.

ACKNOWLEDGMENTS

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